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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Harrington *et al.*

Application No.: Re. 09/586,744

Group Art Unit: 1652

Filed: June 2, 2000

Examiner: T. Saidha

For: MAMMALIAN-SPECIFIC FLAP  
ENDONUCLEASE

Attorney Docket No.: 9584-017-999

**Response to Second Reissue Application Protest**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

Applicant is in receipt of a communication entitled REISSUE APPLICATION PROTEST UNDER 37 C.F.R. 1.291 TO ADDRESS NEW ISSUES dated January 9, 2002 (the "2nd Protest") addressing what the Protester characterizes as "two new issues that could not have been addressed in the previously filed Protest". Although not explained by the Protestor, this second Protest is apparently directed to both the Amendment dated June 15, 2002 and the Communication sent to the Patent Office on November 26, 2001. Applicant submits that this second Protest, like the first, is without merit.

**REMARKS**

**I. The Second Protest is Inadmissible**

The present Protest dated January 9, 2002 is inadmissible because it does not raise substantial new issues relative to the first Protest dated January 3, 2001. In pertinent part, 37 CFR 1.291(c) provides:

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"The limited involvement of the member of the public filing a protest pursuant to paragraph (a) of this section ends with the filing of the protest, and no further submission on behalf of the protestor will be considered, except for additional prior art, or unless such submission raises new issues which could not have been earlier presented.

The present situation is addressed in the Manual of Patent Examination Practice (MPEP 8th Ed. August 2001) at MPEP §1901.03 "Initial Protest Submission Must be Complete":

"A protest must be complete and contain a copy of every document relied on by protestor, whether the document is a prior art document, court litigation material, affidavit, or declaration, etc., because a protestor will not be given an opportunity to supplement or complete any protest which is incomplete. Active participation by protestor ends with the filing of the initial protest, as provided in 37 CFR 1.291(c), and no further submission on behalf of protestor will be acknowledged or considered, except for additional prior art, or unless such submission clearly raises new issues which could not have been earlier presented. Protests which will not be entered in the application file include those further submissions in violation of 37 CFR 1.291(c) by which protestor *merely seeks to participate in the examination process*. For example, *mere arguments relating to an Office action or an applicant's reply would not qualify as a new protest*. Likewise, additional comments seeking to bring in further or even new data or information with respect to an issue previously raised by protestor would not qualify as a new protest. The Office will not add these arguments or comments to the original protest and will not enter them in the application file. (italics added)

The Protestor claims that the second Protest is directed to new issues "that could not have been presented in the previously filed Protest". However, the second Protest is merely a repeat of the Protestor's previous meritless arguments with different wording. There is nothing of substance that could not have been stated in the first Protest.

For example, the "specific incorporation" issue raised by Protestor is not a new one. In the Preliminary Amendment of June 2, 2000, ("Preliminary Amendment"), which is prior to Protester's first Protest, Applicants made the following statement regarding the incorporation by reference:

This reference [Harrington & Lieber, 1995, J. Biol. Chem. 270:4503 ("Harrington & Lieber")] was incorporated into the

specification by reference at Col. 20, line 66 through Col. 21, line 3, and by specific reference to the various DNA flap substrates, cleavage and binding reactions described therein at Col. 39, line 65 through Col. 40, line 3.

(Preliminary Amendment, bottom of page 19 to top of page 20). This statement clearly states that the incorporation of Harrington and Lieber was a specific incorporation so this is not new. Protester has had a full opportunity to raise this issue in its first Protest. There is no reason to justify a second bite at the apple.

Furthermore, the second allegedly new issue pertaining to the naming of double flap structures is improper inasmuch as it relies on Protestor's incorporation by reference arguments, discussed above, and also contains misrepresentations that should be brought to the Examiner's attention.

In the event that the Examiner chooses to enter the second Protest, and to avoid any doubts, Applicant offers the following comments on the alleged "new issues" in the second Protest.

## **II. Incorporation(s) By Reference**

For the first allegedly new issue, the Protestor claims that the Applicant's incorporation by reference is not supported by *In re Voss* (194 USPQ 267, CCPA 1977) and is contradicted by the teachings of the specification. The Protestor argues that *In re Voss* does not support the incorporation by reference in the present case because *Voss* involved an incorporation of glass-ceramic materials that were "merely [known] starting materials" for the claimed strengthening process, whereas the present case involves a double-flap structure that was novel. This is nonsense.

In footnote 2 at the bottom of the fourth page of the second Protest, the Protestor characterizes *In re Voss* as follows: "For example, *In re Voss* identifies a proper incorporation by reference statement as "clearly identifying the subject matter which is incorporated and where it may be found." This is precisely the case in the present specification. At column 39, line 65 to column 40, line 3, the present patent specification states: "DNA flap substrates, cleavage and binding reactions and the like are practiced with reference to the Experimental Examples and ... Harrington and Lieber (1995) *J. Biol. Chem.* 270:4503." Thus, the specification clearly identifies that the subject matter being incorporated concerns flap substrates (among other things), and that this

information can be found in the article by Harrington and Lieber. In fact, it is this information that was properly added by the Preliminary Amendment submitted June 2, 2000, as documented in the tables on pages 20-23 thereof, and in the tables and discussion provided in the Amendment dated June 15, 2001.

Furthermore, Protestor's assertion that the incorporation by reference permitted by *In re Voss* was limited to known starting materials is without merit. Rather, the court in *In re Voss* stated, "It is clear that appellant intended the [incorporated material] to become part of his parent application." (194 USPQ at 270, column 2). This is the case here, in light of the clear references to Harrington and Lieber set forth in the Preliminary Amendment.

The Protestor continues that the incorporation by reference should be barred because incorporation of a double flap structure would be inconsistent with references to 3' flap structures in the specification. The Protestor is wrong.

The Protestor has blatantly mischaracterized the teachings of the specification regarding 3' flap structures. Basically, the specification teaches that 5' flaps are cleaved but not 3' flaps. There is no teaching that a double flap structure cannot be cleaved. The specification teaches that "FEN-1 cleavage is flap strand specific" ('283 specification, Col. 19, line 21), that it has a "5' flap cleavage activity" (Id. Col. 43, lines 40-41), and that it exhibits "specificity for 5' single-stranded flaps." (Id. Col. 47, lines 28-29) (emphasis added). From these teachings, one learns that FEN-1 specifically cleaves 5' single stranded flaps. Thus, FEN-1 specificity is a function of whether the substrate possesses a 5' single stranded flap.

With respect to 3' flaps, at column 46, lines 28-30, the patent specification teaches:

"To test whether FEN-1 cleaves any single-strand/double-strand junction, FEN-1 was assayed for its ability to cleave 5' or 3' overhangs."

At column 46, lines 60-67 under the heading "Ability of FEN-1 to Cleave Other Structures", the specification teaches:

In addition to 5' flap structures, 3' flap structures have also been proposed to serve as intermediates in homology-dependent DNA end-joining. It was of interest, therefore, to test whether FEN-1 also cleaves flaps with a 3' single-stranded end. Using Flap Substrate 1 as a positive control, no detectable cleavage of the 3' flap structure was observed, even in the presence of 15 U of FEN-1.

Taken together, the above passages make clear that what was tested was the ability to cleave 5' or 3' overhangs. Thus, the specification teaches that 3' flaps (or 3' overhangs) are not cleaved, and that 5' flaps (or 5' overhangs) are cleaved. A double flap structure has a 5' flap, and the specification teaches that 5' flaps are cleaved. Accordingly, the teachings of the '283 specification are consistent with the incorporation and claiming of double flap structures.

Finally, the Protestor's discussion of *In re Kaslow* is without merit as well, since cleavage of the 5' flap in a double flap structure is not contradicted by failure to cleave a 3' flap.

### **III. Double Flap Structures**

Protester alleges that Applicant cannot classify a double-flap structure as a 5' flap structure. Of course, Protester sees no problem with classifying a double-flap structure as a 3' flap structure. The definition of both 5' flap structures and 3' flap structures appear in the '283 specification, and, according to these definitions, a double-flap structure actually qualifies as both. Protester has provided no reasoning to support the unequal application of the 3' flap definition over the 5' flap definition. No such reason exists.

Protester takes issue with the term "5',3'-double flap structure" used by Applicants. This term is supported by both the very structure of the double flap substrate, as well as the following text from Harrington & Lieber: "This substrate, called a double flap structure, contained both a 5'- and a 3'-flap strand." (Harrington & Lieber, page 4506, first column, lines 13-14). In addition, since the '283 specification uses the terms "3'-flap structures" and "5'-flap structures," the term "5'-3'-double flap structure" is a convenient name that is consistent with the nomenclature used in the '283 specification for the flap substrates. Applicants submit that use of the term "5',3'-double flap structure" is appropriate, and is supported by specification and Harrington & Lieber. Whether a

double flap structure is called a 5',3'-double flap structure or a 3',5'-double flap structure is immaterial – they mean the same thing.

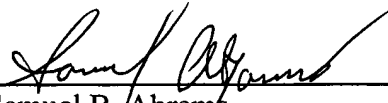
#### IV. CONCLUSION

As evidenced by the above discussion, the second Protest is without merit. Withdrawal of the present rejections and allowance of the application are respectfully requested.

Respectfully submitted,

Date

May 28, 2002

  
Samuel B. Abrams

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(Reg. No.)

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